

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

Claim 1. (Currently Amended): A method of examining the physiological effect of a compound on a mammalian prostate cancer cell, comprising:

(a) contacting said compound to be tested with said mammalian prostate cancer cell, wherein said mammalian prostate cancer cell expresses an exogenous wild type androgen receptor polynucleotide that encodes an androgen receptor polypeptide or an androgen receptor polypeptide variant, such that a total level of mRNA in the cell that encodes said androgen receptor polypeptide or said androgen receptor polypeptide variant, or a total polypeptide level of said androgen receptor polypeptide or said androgen receptor polypeptide variant, is at least two-fold higher than the endogenous level of androgen receptor mRNA or polypeptide in a hormone-sensitive prostate cancer cell, and wherein growth of said mammalian prostate cancer cell is ~~androgen-independent~~ hormone refractory, to provide a treated prostate cancer cell;

(b) comparing one or more physiological characteristics of said treated prostate cancer cell with the same one or more characteristics of a control prostate cancer cell to which said compound has not been administered; and

(c) determining from a difference in the one or more characteristics whether said compound has a physiological effect on the treated prostate cancer cell, decreases the biological function of androgen receptors, and/or inhibits the growth of hormone-refractory prostate cancer cells.

Claims 2.-4. (Canceled)

Claim 5. (Currently Amended): A method of examining a physiological effect of a compound on a selected mammalian cancer cell wherein said cancer cell stably expresses an exogenous wild type polynucleotide that encodes a nuclear receptor protein or polypeptide, said cell further comprising an increased level of mRNA that encodes said nuclear receptor protein or

polypeptide when compared to an endogenous level of mRNA that encodes said nuclear receptor protein or polypeptide in a hormone-sensitive mammalian cancer cell, said method comprising:

- (a) determining that said increased level of mRNA in said selected mammalian cancer cell is at least two fold higher than the endogenous level of mRNA in said hormone-sensitive mammalian cancer cell;
 - (b) contacting the compound to be tested with said selected mammalian cancer cell to provide a treated cancer cell;
 - (c) examining one or more physiological characteristics of said treated cancer cell;
- and
- (d) determining from the one or more physiological characteristics that said treated cancer cell has the one or more physiological characteristics,

wherein the growth of said selected mammalian cancer cell is nuclear receptor ~~ligand-~~
independent ligand refractory.

Claim 6. (Withdrawn): A method of examining the physiological effect of a compound on a selected mammalian cancer cell wherein said selected cancer cell expresses an exogenous wild type polynucleotide that encodes an abnormal level of protein or polypeptide of interest when compared to the endogenous level of said protein or polypeptide of interest encoded by a hormone-sensitive mammalian cancer cell, said method comprising:

- (a) determining that said abnormal level of said protein or polypeptide of interest is at least two fold higher than the endogenous level of said protein or polypeptide of interest in said hormone-sensitive mammalian cancer cell;
- (b) contacting a compound to be tested with said selected cancer cell to provide a treated cancer cell; and
- (c) examining one or more physiological characteristics of said treated cancer cell.

Claim 7. (Previously Presented): A method of examining the physiological effect of the compound on the selected mammalian cancer cell according to claim 5 which includes the additional steps of:

(e) providing a mammalian cancer cell which is the same as said selected mammalian cancer cell and which is not contacted with said compound to thereby provide a control cancer cell;

examining said one or more physiological characteristics of said control cancer cell; and

comparing said one or more physiological characteristics of said control cancer cell with said one or more physiological characteristics of said treated cancer cell.

Claim 8. (Withdrawn): A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 6 which includes the additional steps of:

(d) providing a mammalian cancer cell which is the same as said selected cancer cell and which is not contacted with said compound to thereby provide a control cancer cell;

examining said one or more physiological characteristics of said control cancer cell; and

comparing said one or more characteristics of said control cancer cell with said one or more characteristics of said treated cancer cell.

Claim 9. (Previously Presented): A method of examining the physiological effect of the compound on the selected mammalian cancer cell according to claim 5, wherein said selected mammalian cancer cell is selected from the group consisting of breast cancer cells, ovarian cancer cells and prostate cancer cells.

Claim 10. (Withdrawn): A method of inhibiting the growth of hormone refractory prostate cancer cells wherein said cells comprise androgen receptors that exhibit biological function, said method comprising the step of decreasing the biological function of said androgen receptors.

Claims 11.-15. (Canceled)

Claim 16. (Withdrawn): A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 10 wherein the androgen receptor protein is decreased by

modifying the polynucleotide or polypeptide sequence of the androgen receptor or by posttranslational modifications of the androgen receptor selected from the group consisting of phosphorylation, acetylation, ubiquitination, and sumolation.

Claim 17. (Withdrawn): A method for determining if a selected prostate cancer cell is hormone sensitive or has become hormone refractory, said method comprising the steps of:

- (a) determining the level of mRNA in said selected cell that encodes the androgen receptor polypeptide or androgen receptor polypeptide variant;
- (b) determining the level of mRNA in a hormone sensitive selected prostate cancer cell;
- (c) comparing the level of mRNA determined in step (a) to the level of mRNA determined in step (b); and
- (d) determining that the selected prostate cancer cell is hormone sensitive or has become hormone refractory if the level of mRNA determined in step (a) is at least two fold higher than the level of mRNA determined in step (b).

Claim 18. (Withdrawn): A method for determining if a selected prostate cancer cell is hormone sensitive or has become hormone refractory, said method comprising the steps of:

- (a) determining the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant in said selected cell;
- (b) determining the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant in a hormone sensitive selected prostate cancer cell;
- (c) comparing the level of androgen-receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (a) to the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (b) and
- (d) determining that the selected prostate cancer cell is hormone sensitive or has become hormone refractory if the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (a) is at least two fold higher than the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (b).

Claim 19. (Withdrawn): A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 6 wherein said selected mammalian cell is selected from the group consisting of breast cancer cells, ovarian cancer cells and prostate cancer cells.

Claim 20. (Previously Presented): The method of claim 1, wherein said compound modulates a signal transduction pathway to decrease androgen receptor protein levels.

Claim 21. (Previously Presented): The method of claim 1, wherein said compound induces cellular degradation pathways.

Claim 22. (Previously Presented): The method of claim 1, wherein said compound dissociates the androgen receptor polypeptide or the androgen receptor polypeptide variant from heat shock proteins that maintain androgen receptor integrity.

Claim 23. (Previously Presented): The method of claim 1, wherein said compound is an androgen receptor antisense mRNA molecule.

Claim 24. (Previously Presented): The method of claim 1, wherein the total level of mRNA in the mammalian prostate cancer cell that encodes said androgen receptor polypeptide or said androgen receptor polypeptide variant, or the total polypeptide level of said androgen receptor polypeptide or said androgen receptor polypeptide variant, is at most five-fold higher than the endogenous level of androgen receptor mRNA or androgen receptor polypeptide in the hormone-sensitive prostate cancer cell.

Claim 25. (Previously Presented): The method of claim 20, wherein said compound targets EGF receptors that crosstalk to an androgen receptor.

Claim 26. (Previously Presented): The method of claim 1, further comprising assaying said compound for decreasing the biological function of androgen receptors by decreasing an androgen receptor DNA level, androgen receptor mRNA level, and/or androgen receptor protein level.

Claim 27. (Previously Presented): The method of claim 5, further comprising assaying the compound to be tested for decreasing the level of mRNA that encodes said nuclear receptor protein or polypeptide.

Claim 28. (Currently Amended): The method of claim 5,
wherein the nuclear receptor protein is selected from the group consisting of the androgen receptor protein and the estrogen receptor protein and
wherein the nuclear receptor ~~ligand-independent~~ ligand refractory growth of said selected mammalian cancer cell is selected from the group consisting of ~~androgen-independent~~ androgen refractory growth and ~~estrogen-independent~~ estrogen refractory growth.